



NDA 213411/S-004

## **ACCELERATED APPROVAL**

Seagen Inc.  
Attention: Riddhi Virparia, Pharm.D., R.A.C.  
Associate Director, Regulatory Affairs  
21823 30th Drive SE  
Bothell, WA 98021

Dear Dr. Virparia:

Please refer to your supplemental new drug application (sNDA) dated July 19, 2022, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TUKYSA (tucatinib) tablets.

This Prior Approval supplemental new drug application adds a new indication of TUKYSA in combination with trastuzumab for the treatment of adult patients with RAS wild-type, HER2-positive, unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy.

### **APPROVAL & LABELING**

We have completed our review of this application. It is approved under the provisions of accelerated approval regulations (21 CFR 314.500), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

### **WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

### **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at

FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(I)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **ACCELERATED APPROVAL REQUIREMENTS**

Products approved under accelerated approval pursuant to Section 506(c) of the FDCA and 21 CFR 314.510, may require further adequate and well-controlled clinical trials intended to verify and describe clinical benefit. You are required to conduct such clinical trials with due diligence. If required postmarketing clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated January 5, 2023. This requirement, along with required completion dates, is listed below.

4388-1      Conduct a randomized clinical trial to obtain data on the clinical efficacy of tucatinib for patients with RAS wild type, HER2-positive, unresectable or metastatic colorectal carcinoma. The trial should compare tucatinib in combination with trastuzumab with the standard of care in patients with RAS wild type, HER2-positive, unresectable or metastatic colorectal carcinoma. The primary endpoint should be progression-free survival (PFS) per blinded assessment or overall survival. The trial should enroll a sufficiently representative study population to reflect the racial and ethnic diversity of the U.S. patient population with RAS wild type, HER2-positive, unresectable or metastatic colorectal carcinoma and allow for interpretation of the results across this representative study population.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

Trial Completion: 10/2025  
Final Report Submission: 04/2026

Submit clinical protocols to your IND 134840 for this product. In addition, you must submit status reports of the progress of each requirement not later than 180 days after the date of approval of this drug and every 180 days thereafter (section 506(B)(a) of the FDCA as amended by section 3210(b) of the Food and Drug Omnibus Reform Act of 2022). Under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each requirement in your annual report to this NDA. The status summary should include expected trial completion and final report submission dates, any changes in plans since the last report, and, for clinical trials, the number of patients entered into each trial.

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this post marketing requirement must be clearly designated “**Subpart H Postmarketing Requirement(s).**”

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

### **POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitments:

4388-2      Submit adequate analytical and clinical validation results from clinical trial data to support labeling of a test to detect HER2 overexpression or gene amplification, that is essential to the safe and effective use of tucatinib in patients with HER2-positive colorectal cancer.

The timetable you submitted on January 5, 2023, states that you will conduct this study according to the following schedule:

Trial Completion: 10/2025

**U.S. Food and Drug Administration**  
Silver Spring, MD 20993  
[www.fda.gov](http://www.fda.gov)

Final Report Submission: 04/2026

Submit clinical protocols to your IND 134840 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients/subjects entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **“Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,” or “Postmarketing Commitment Correspondence.”**

### **PROMOTIONAL MATERIALS**

Under 21 CFR 314.550, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 314.550, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>3</sup>

### **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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<sup>3</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

If you have any questions, call Nataliya Fesenko, Pharm.D., Regulatory Health Project Manager, at (240) 402-6376.

Sincerely,

*{See appended electronic signature page}*

Lola Fashoyin-Aje, M.D., M.P.H  
Deputy Director  
Division of Oncology 3  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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